

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in this application.

Listing of Claims

1. (Currently amended) A method of determining the frequency of an allele in a population of nucleic acid molecules, said method comprising:

pooling the nucleic acid molecules of said population to provide a pooled nucleic acid sample; performing primer extension reactions in a reaction mixture comprising said pooled nucleic acid sample and a primer which binds at a predetermined site located in said nucleic acid molecules, wherein said site is substantially adjacent to a polymorphic position of interest in said allele, to provide primer extension products, and wherein the primer extension reaction is performed by sequentially adding non-chain terminating nucleotides to the reaction mixture and quantitatively determining the incorporation or non-incorporation of each nucleotide as each nucleotide is added by bioluminometrically detecting the release of pyrophosphate; obtaining a pattern of nucleotide incorporation in said primer extension products at the positions that correspond to said polymorphic position of interest; and determining the frequency of said allele from said pattern of nucleotide incorporation.

2. (Cancelled).

3. (Cancelled).

4. (Cancelled).

5. (Currently amended) The method according to ~~claim 4~~ claim 1 wherein ELIDA detection enzymes are used to detect the release of pyrophosphate.

6. (Previously presented) The method according to claim 5 wherein a nucleotide-degrading enzyme is included during the primer extension reaction.
7. (Original) The method according to claim 1 wherein the nucleic acid molecules are immobilized on a solid support.
8. (Original) The method according to claim 1 wherein the amount or concentration of the nucleic acid in each sample of the population which is pooled, is determined prior to pooling.
9. (Previously presented) The method according to claim 8 wherein the concentration of the nucleic acid in each sample of the population is determined by a primer-extension reaction prior to pooling.
10. (Original) The method according to claim 9 wherein the volume of each nucleic acid in each sample to be pooled is adjusted in view of the amount or concentration of nucleic acid present such that the pooled sample contains substantially the same amount or concentration of each nucleic acid molecule in the population.
11. (Previously presented) The method according to claim 10 wherein a particular polymorphism is selected as a reference polymorphism and said primer extension reaction used to determine the concentration of nucleic acid in said sample is specific for said reference polymorphism.
12. (Original) The method according to claim 11 wherein said polymorphism is chosen such that it gives no background signals in a primer-extension reaction and that the signals are even.

13. (Previously presented) The method according to claim 11 wherein said polymorphism is not present in a homopolymeric sequence and will not be preferentially amplified in any PCR-type reactions.

14. (Previously presented) The method according to claim 11 wherein a reference sample containing said polymorphism is selected as the main reference from one of the homozygotes of one of the alleles of said polymorphism (Ref 1) and another reference (Ref 2) containing said polymorphism is selected from the other homozygote, and the reference samples are pooled and primer extension reactions are performed, and the pattern of nucleotide incorporation determined to determine the relative concentration of each reference sample.

15. (Previously presented) The method according to claim 14 wherein the sample nucleic acid molecules to be tested are pooled individually with the reference samples.

16. (Cancelled).

17. (Currently amended) A method of determining the amount of an allele in a sample of nucleic acid molecules, said method comprising:

performing primer extension reactions in a reaction mixture comprising said nucleic acid molecules, using a primer which binds at a predetermined site located in at least one said molecule wherein said site is substantially adjacent to a polymorphic position of interest in said allele, to provide primer extension products, and wherein the primer extension reaction is performed by sequentially adding non-chain terminating nucleotides to the reaction mixture and quantitatively determining the incorporation or non-incorporation of each nucleotide as each nucleotide is added by bioluminometrically detecting the release of pyrophosphate; determining the type and number of nucleotides incorporated in said primer extension products at positions that correspond to the polymorphic position of interest, and determining the amount of occurrence of said allele in said sample by analyzing the type and number of nucleotides incorporated.

18. (Cancelled).

19. (Cancelled).

20. (Cancelled).

21. (Currently amended) The method according to claim ~~20~~ 17 wherein ELISA detection enzymes are used to detect the release of pyrophosphate.

22. (Previously presented) The method according to claim 21 wherein a nucleotide-degrading enzyme is included during the primer extension reaction.

23. (Original) The method according to claim 22 wherein the nucleic acid molecules are immobilized on a solid support.

24. (Cancelled).

25. (Cancelled).